Presentation | 02 Rupert Handgretinger, M.D., Ph.D.

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EDUCATION AND ACADEMIC DEGREES

Baccalaureate	1974	Wieland-Gymnasium Biberach, Germany
M.D.	1986	Medical School at University of Tübingen, Germany
Ph.D.	1996	Medical School at University of Tübingen, Germany

PROFESSIONAL APPOINTMENTS, ACADEMIC ACHIEVEMENTS

1989 - 2000	Director of the Stem Cell Transplantation Lab, Children's University Hospital, Tübingen.
2000 - 2005	Endowed Chair (tenure) of the Division of Stem Cell Transplantation, Department of Hematology/Oncology, St. Jude Hospital Children's Research Hospital, Memphis
2000 - 2005	Full Faculty Member, SJCRH
2002 - 2005	Professor of Pediatrics, Department of Pediatrics, The University of Tennessee, Health Science Center, Memphis
2000 - 2005	Co-Program Leader of the Cell and Gene therapy Program, SJCRH
2002 - 2005	Medical Director of the Human Applications Lab with FACT accreditation
2005 - present	Chairman of the Department of Hematology/Oncology and General Pediatrics, Children's University Hospital, Tübingen

PUBLICATIONS

322 Published Papers in the Peer Reviewed Journals

The role of BioBran (RBAC) in NK-cell mediated anti-tumor treatment strategies in pediatric cancer

Natural Killer (NK) cell cytotoxic activity is crucial in fighting viral infections and controlling of malignant diseases. Low NK activity is associated with high relapse rate in pediatric patients with leukemia after stem cell transplantation. BioBran (RBAC) has been described as a potent enhancer of NK cell activity against a variety of tumors like breast cancer and hepatocarcinoma. However no data has been reported in pediatric tumors. Here we show that overnight stimulation with BioBran (RBAC) increased NK cell cytotoxic activity against leukemic cell lines (K562, Jurkat) and against various neuroblastoma and sarcoma cell lines (NB1691, A673, A204, RD and RH30 cell lines) *in vitro*. We could demonstrate a synergistic effect of low dose Interleukin-2 (IL-2, 40 IU/ml) and BioBran (RBAC) on cytotoxic activity of NK cells, which was comparable to high dose IL-2 (1000IU/ml). Furthermore, in an *in-vivo* xenograft model of neuroblastoma BioBran (RBAC) stimulated NK cells were able to decelerate neuroblastoma growth and increase survival. Beside the effect on cytotoxic activity of NK cells we could also show that BioBran (RBAC) enhances the proliferative potential of IL-2 and IL-2 and IL-15 stimulated NK cells *in vitro*. Thus, the combination of IL-2 and BioBran (RBAC) could be a promising approach to augment NK activity and proliferation in pediatric patients. We therefore tested the effect of orally administered BioBran (RBAC) (3 x 1 sac./day) in healthy volunteers and could also demonstrate an effect on NK activity whereas no effect was seen on NK cell count. In pediatric patients we obtained different results with an increase of NK activity in 6 patients and no effect in 4 patients. Especially in patients with active disease, NK activity was low and could not be enhanced with BioBran (RBAC). In three patients so far we combined oral BioBran (RBAC) (3 x 2 sac./day) with subcutaneously administered IL-2 (1 x 10^6 IU/m^2, thrice a week). The combination was well tolerated and led to an increase in NK activity. The mechanism by which BioBran (RBAC) stimulates NK cells is still not well understood. We could demonstrate TLR-signalling only for TLR-4 which could be caused by LPS contained in BioBran (RBAC). However, neutralizing LPS with polymyxin B did not abrogate the stimulating effect of BioBran (RBAC) on NK activity. Further research to identify the exact intracellular mechanism will help to optimize the effect of BioBran (RBAC) in a clinical setting.